Amendments to the Drawings

The attached sheets of drawings include changes to FIG. 4 and FIG. 5. The handwritten labels have been replaced with typeset labels. No other amendments have been made.

Remarks

Claims 1-12, 14-18, and 52-60 were pending in this application. Claims 9-12, 16, 52, and 58-60 were withdrawn from consideration by the Examiner. Claim 1 is amended herein to correct form. Claims 2, 4, 6 and 55 are amended to correct dependency. Claims 14, 15, 17 and 18 are amended herein to refer to SEQ ID NO: 1, which was elected in response to the restriction requirement. Please cancel claims 3, 5 and 52, without prejudice to renewal.

Applicants believe no new matter is added herein. Applicant has made every effort to address each of the rejections asserted in the Office action, in the order listed in the action. Reconsideration of the subject application is respectfully requested.

Restriction Requirement

Applicants respectfully disagree with the restriction requirement, for the reasons of record. Applicants submit that the claimed polypeptide and the claimed polynucleotides in the present applicant share a special technical feature. However, Applicants submit that all of the claimed proteins share a special technical feature, namely that they include 8 to 11 contiguous amino acids of SEQ ID NO: 1. Thus, there is unity of invention, as the proteins all exhibit a shared special technical feature, and the claimed nucleic acids encode those proteins. Applicants expressly reserve the right to petition the restriction requirement.

Objection to the Drawing

The Examiner has objected to the drawing submitted with the prior Office action. This objection was discussed with Examiner Davis on March 13, 2006. Applicants thank Examiner Davis for the helpful telephone conference, and apologize for the typographical error made in the drawings submitted on September 2, 2004.

It is the Applicants understanding of the Office action that the replacement drawings (incorrectly labeled "FIG. 5" and "FIG. 6") submitted on September 2, 2004 were not entered into the specification. Thus, replacement drawings, correctly labeled "FIG. 4" and "FIG. 5" accompany this response. In these figures, the handwritten labels have been replaced with typeset labels. No additional amendments have been made to the figures.

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-8, 14-15, 17-18 and 54-57 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly being indefinite for the term "the peptide." Claim 1 is amended herein to recite "the polypeptide," as suggested in the Office action, rendering the rejection moot.

Rejection Under 35 U.S.C. § 112, first paragraph

Written Description

Claims 1-8, 14-15, 17-18 and 54-57 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly there is insufficient written description for the claimed subject matter.

The Office action alleges that claims 14-15 and 17-18, in the recitation of "PAGE4" encompass proteins for which there is insufficient written description in the specification. Applicants respectfully disagree with this assertion. However, in the interest of advancing prosecution, claims 14-15 and 17-18 are amended to refer to "SEQ ID NO: 1," rendering the rejection moot.

The Office action states that there is insufficient written description for 8 to 11 consecutive amino acids of SEQ ID NO: 1 that bind to MHC class I or that could elicit an immune response. The Office action further asserts that there is no teaching in the specification of any structural feature of PAGE4 polypeptides that bind MHC, nor is there any correlation between structure and function between the claimed peptides that could induce a cytotoxic T cell response. Applicants respectfully disagree with this assertion.

To satisfy the written description requirement, a patent application must describe an invention in sufficient detail that one skilled in the art can clearly conclude that the inventor was in possession of the claimed subject matter. The case cited in the Office action, (Regents of the *University of California v. Eli Lilly & Co.,* 119 F. 3d 1559, 43 USPQ2d (Fed. Cir. 1997)) is directed to patents that disclose nucleic acid sequences. The claims at issue were broadly directed to "vertebrate," "mammalian," and "human" insulin cDNA. Only a rat cDNA was provided in support of the claim. The claims in that decision are dramatically different from the claims in the subject application.

In the present application, the claims are directed to 8 to 10 consecutive amino acids of SEQ ID NO: 1 (a 102 amino acid sequence); the claims are not broadly directed to molecules from other species. In addition, the claims are limited to polypeptides having a specified

function, namely that they bind MHC, and can be used to induce an immune response. Thus, the disclosure of the present application is more detailed, and the claims are more narrow in scope, that the claims at issue in *University of California v. Eli Lilly & Co.*

The U.S. PTO's own guidelines on written description explain that the policy goals include (i) clearly conveying to the public what was invented, (ii) putting the public in possession of the applicant claims as the invention. The specification includes sufficient written to meet these goals. Specifically, the complete amino acid sequence of PAGE4 is shown in SEQ ID NO: 1 and FIG. 5 of the specification. Functional domains of SEQ ID NO: 1 are disclosed in on pages 14-15, which describes similarity of the amino acid sequence set forth as SEQ ID NO: 1 (PAGE4) with GAGE and MAGE proteins, and discloses the presence of RGD motifs (which are disclosed to be involved in protein-protein interactions) in SEQ ID NO: 1. The specification clearly describes immunogenic epitopes of PAGE4 in a sufficient detail to clearly convey to the public what was invented and to put the public in possession of what the applicant claims as the invention. For example, immunogenic peptides, such as peptides that bind MHC are disclosed in the specification on page 7, line 35 to page 8, line 25, and on page 20, line 1 to page 22, line 5. The specification also discloses that epitopes of use are 8-10 amino acids in length and have anchoring residues, such as at positions 2 and 9 of the PAGE4 polypeptide, see page 20, lines 33-34). Specific types of PAGE4 polypeptides that are of specific use are disclosed. For example, it is disclosed that the PAGE4 polypeptides can be 9 or 10 amino acids in length and can include binding motifs for HLA-A2 (see, for example, page 8, lines 30-37; page 20, to page 21, line 2, and page 21, lines 15-19).

The Office action cites to *University of California v. Eli Lilly & Co.* (see page 10 of the Office action) as holding that "the instant specification may provide an adequate written description of the claimed polypeptides that bind major histocompatibility complex (MHC) I, or that could induce a CTL response.....by describing structural features common to members of the genus." The Office action further cites to *Enzo Biochem, Inc. v. Gen-Probe, Inc., 296* F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002) as stating that the specification can provide disclosure of "sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled to known or disclosed correlation between function and structure, or some combination of such characteristics." Applicants believe that the present specification meets these requirements. Peptides are described that have specific anchoring residues in the second position (A, L, I, V, M or S) and a positively charged amino acid at the position nine (see page 20, line 20

to page 21, line 2). The selection of binding motifs that bind HLA-A2 (the specified function of binding MHC class I) is disclosed on page 28, line 25 to page 29, line 29. In addition, biological methods to test whether a specific epitope is immunogenic are provided (for example, see page 8, lines 1-4 and page 21, lines 3-12 and lines 20-29). Further, as discussed above, reference to specific algorithms for identifying peptides that bind MHC are provided in the specification.

Applicants take this opportunity to note that information that is well known to those of skill in the art need not be included in the application, and "preferably is omitted (see In re Buchner, 929 F.2d 660, 18 USPQ2d 1331 (Fed. Cir. 1991)). Computer programs for predicting MHC binding were well known to those of skill in the art at the time the provisional application was filed (see for example, Parker et al., Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-chains. J Immunol 152:163-75, 1994). However, considerable supporting information is also provided in the specification, for example methods and computer based programs for predicting MHC binding motifs (immunogenic epitopes) are disclosed in the specification (for example, see page 8, lines 12-25 and page 21, line 34 to page 22, line 5). Thus, the specification clearly provides sufficient starting materials for carrying out a process (see *Genentech, Inc. v. Novo Nordisk*, 108 F.3d 1361, 1366, 42 USPQ2d 1001, 1005 (Fed. Cir. 1997)). Thus, Applicants submit that sufficient written description is provided for immunogenic peptides of eight to ten consecutive amino acids in length of SEQ ID NO: 1 that specifically bind MHC.

In support of this assertion, attached herewith is the declaration of Dr. Pastan. This declaration documents that using the description provided by the specification, he and his colleagues (who are of skill in the art) were able to generate immunogenic PAGE4 polypeptides, and use these polypeptides to activate cytotoxic T cells. Cytotoxic T cells activated using the immunogenic PAGE4 polypeptides were able to lyse prostate cancer cells expressing PAGE4. Applicants submit that this declaration documents that one of skill in the art, given the guidance provided by this specification, could make and use the claimed polypeptides.

In view of these remarks, and the Declaration of Dr. Pastan, reconsideration and withdrawal of the rejection under 35 U.S.C. § 112, first paragraph are respectfully requested.

Rejection Under 35 U.S.C. § 101

Utility

Claims 1-8, 14-15, 17-18 and 53-57 are rejected as allegedly there is no utility for the claimed polypeptides. Applicants respectfully disagree with this rejection as may be applied to the pending claims.

The Office action states that one cannot determine that SEQ ID NO: 1 could be used for diagnosis or treatment of cancers. However, the Office action acknowledges (see page 14) that the polynucleotide encoding SEQ ID NO: 1 is differentially expressed in prostate and uterine cancers as compared to controls, as "protein levels cannot be predictably correlated with steady-state mRNA levels." In support of this assertion the Office action cites:

1. Brennan et al., directed to detection of TNF alpha in synovial cells,
2. Zinner et al., documenting the mRNA level of S100 (a protein that is calcium modulated), and showing that this protein is post-transcriptionally regulated
3. Eriksson et al., which teaches a lack of correlation of mRNA with protein from an insulin responsive glucose transporter
4. Hell et al., on the presence of bcl-2 mRNA in Hodgkin's cells,
5. Guo et al., describing Oatp2 in the liver is regulated at both the transcriptional level and the translational level

Only one of these references (Hell et al.) describes a comparison of mRNA and protein in tumor cells, and none of the references describe results obtained in carcinomas. Thus most, if not all, of the cited references are irrelevant to determining the correlation of protein levels with mRNA levels in tumor cells.

Applicants note that Ornstoft et al., Molec. Cell Proteomics 1: 37-45, 2002 (copy submitted herewith as Exhibit A) describes a genome-wide study of gene copy numbers, transcripts and protein levels in pairs of non-invasive and invasive human carcinomas. Although it was only possible to compare mRNA and protein in a few cases (due to a limited ability to focus some of the proteins on two dimensional gels), there was a good correlation ($p<0.005$) between transcript alterations and protein levels.

Moreover, submitted herewith is the Declaration of Dr. Pastan. This declaration describes that Northern blot and reverse transcriptase polymerase chain reaction (see page 4, line 30 to page 5, line 6; page 5, lines 16-20; and FIGs. 3 and 5) were used to evaluate the expression of PAGE4 in prostate cancer. Polyclonal antibodies (see Example 3, page 41 of the

specification) were used to determine if PAGE4 protein was expressed in prostate cancer. Western blot analysis confirmed that PAGE4 was expressed in a prostate cancer lysate (see Fig. 2B of Iavrone et al., Mol. Cancer Therap. 1: 329-335, 2002, copy submitted herewith as Exhibit B, for an exemplary blot). Samples of prostate cancer from five patients whose cancers expressed PAGE4 mRNA were analyzed to confirm that PAGE 4 protein was expressed. PAGE4 protein was expressed in all five of these samples (a 100% correlation). This specific data with respect to PAGE4 prostate tumor expression is more convincing than general allegations based on prior art references.

The Office action further asserts that as cancer treatment is unpredictable, as there is a problem with tumor tolerance and loss of class I MHC, that there can not be any utility in using immunogenic fragments of SEQ ID NO:1. Similarly, it is alleged that one cannot predict that an immunogenic fragment can be used to recognize and lyse malignant cells (see page 15). In support of this assertion, the Office action refers to Smith, Clin. Immunol. 41:841-9, 1994. Smith (which was published in 1994, four years prior to the filing date of the parent provisional application), describes that a surveillance function of the immune system fails when nascent tumors are formed. Smith et al. describes the use of tumor infiltrating lymphocytes taken from a subject's own tumor, and inserting a gene encoding a full-length tumor specific antigen into the tumor cells themselves, and describes some difficulties with this system. However, Smith et al. describes that there are "new" studies, "such as with MAGE-1 in melanoma, that can potentially be used to augment T cell responses incorporated into vaccine complexes or into viral vectors" (see page 847). Thus, Smith et al., four years prior to the priority date, acknowledges that the use of tumor antigens, or fragments of tumor antigens, can potentially be of use in treatment.

The Office action further cites to Boon, Adv. Canc. Res. 58: 177-210, 1992, as showing that immune tolerance can occur in cancer. However, Boon et al. state "it is now generally accepted that T lymphocytes are the key specific element of the specific immune response directed against tumor rejection antigens. For several tumor antigens, it is possible to obtain from syngeneic animals highly specific cytotoxic T lymphocytes..." (page 179). Boon et al. does disclose that animals with a large tumor burden can be tolerized to tumor antigens, and suggest that tolerance may need to be broken if a patient is unresponsive (see page 207). However, pointing out that there may be problems with an approach does not negate the approach. Boone et al. state that they believe that once tumor rejection antigens are identified

and isolated "they can be used for active immunization to elicit antitumoral response in cancer patients (see page 205, under "Perspectives").

Similarly, the Office action cites to Ezzel (J. NIH Res. 7: 46-49, 1995), and Spitler (Cancer Biotherapy 10: 1-3, 1995) as providing negative statement suggesting that cancer vaccines will not work. Applicants do not deny that for every emerging field (both Ezzel and Spitler were published 3 years prior to the filing date of the present application) there are those who believe a therapy will not work, nor do they deny that for some cancer patients a proposed therapeutic protocol may not function. But that does not mean that claimed polypeptides and methods have no utility.

Indeed, the U.S. Patent and Trademark Office appears to agree that a claimed peptide can have utility for treating a specific type of cancer. For example, U.S. Patent No. 6,756,038 discloses specific carcinoembryonic antigen polypeptides and their use to induce an immune response against carcinomas. U.S. Patent No. 7,005,498 describes MUC1 polypeptides and their use to induce an immune response against cancer. U.S. Patent No. 6,419,931 describes immunogenic compositions comprising antigenic epitopes of viral proteins that bind HLA and their use to treat cancer. Thus, it appears that antigenic peptides and their use to induce an immune response to either a specific tumor (as in the case of U.S. Patent No. 6,756,038) or against a variety of cancers (as in the case of U.S. Patent No. 6,419,931) have a specific and credible utility.

The Office action states that the specification teaches that SEQ ID NO: 1 has some similarity to MAGE proteins, but that there is no teaching of any peptide that is the same as in MAGE proteins (see page 17). The Office action further asserts that as a single publication on MAGE proteins, namely Krkin et al. (APMIS 016: 665-679, 1998), documents that a single MAGE protein (specifically EVDPIGHLY) has only limited anti-tumor activity, then the claimed polypeptides cannot have any utility. Based on this "evidence," the Office action asserts that the claimed PAGE4 polypeptides cannot be of use.

However, there are many references that support the idea that MAGE proteins have a specific and credible use. For example, U.S. Patent No. 5,554,724 describes and claims immunogenic MAGE-2 proteins that specifically bind MHC. U.S. Patent No. 6,051, 237 describes and claims vaccines for inducing an immune response to a tumor, including the use of vectors that express MAGE-1 (see claim 2). U.S. Patent No. 6,392,016 describes MAGE-B proteins and peptides, and discloses their use in treating cancer. Thus, it appears that the U.S.

PTO has previously considered the MAGE proteins to have a specific and credible utility. Applicants would also like to point out that a comparison of PAGE, MAGE, and GAGE proteins, showing specific amino acid comparisons, is provided in FIG. 1. It is not the Applicants' intention to claim MAGE polypeptides, nor is it the Applicants' intention to argue that PAGE has exactly the same function or structure as MAGE (as appears to be suggested on page 19 of the Office action, which describes potential pitfalls of predicting function and three dimensional structure based on sequence comparison). The information on MAGE is provided to show that, if one takes into consideration data on MAGE polypeptides, one of skill in the art would believe that disclosed utility is both specific and credible.

The Office action further asserts that even if CTLs could be produced, it cannot be predicted that they would recognize and lyse malignant cells expressing SEQ ID NO: 1. This argument is asserted under the heading of the utility rejection; thus it is the Applicants understanding that the Office action is alleging that activated CTLs have no use in treating cancer. Applicants respectfully disagree with this assertion. Applicants note that specific CTL clones that bind MAGE and their use are disclosed and claimed in U.S. Patent No. 6,407,063, documenting the utility of CTLs that specifically recognize tumor antigens.

In support of the assertion that the claimed polypeptides can be used to induce an immune response, and have a specific and credible use, submitted herewith is the Declaration of Dr. Pastan. The work described in this declaration documents that a polypeptide of nine consecutive amino acids of SEQ ID NO: 1 can be used to activate cytotoxic T cells. These T cell can lyse prostate cancer cells *in vitro*. This data supports the therapeutic utility of the claimed polypeptides.

In view of these remarks, and the Declaration of Dr. Pastan, reconsideration and withdrawal of the rejections under 35 U.S.C. § 101 are respectfully requested.

Rejections Under 35 U.S.C. § 112, first paragraph

Enablement

Claims 1-8, 14-15, 17-18 and 54-57 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly not being enabled by the specification. Applicants respectfully disagree with this assertion.

In determining whether a patent application is in compliance with the enablement requirement, it must be considered whether one of ordinary skill in the art could practice the claimed invention without undue experimentation (In re Wands, 858 F.2d 731, 8 USPQ 1400 (Fed. Cir. 1988)). In this context, Applicants provide the following Wands analysis:

1. The breadth of the claims

The claims are limited to polypeptides comprising SEQ ID NO:1, or to polypeptides consisting of eight to ten amino acids of SEQ ID NO: 1 that bind MHC. Thus, the scope of the claims are limited to a single amino acid sequence of 102 amino acids, and a limited number of fragments of this single amino acid sequence that can bind MHC class I.

2. The nature of the invention

The invention is limited to specific amino acid sequences. Methods for synthesizing amino acid sequences are routine and/or automated.

3. The state of the prior art

The prior art teaches how to identify immunogenic epitopes of a specified protein sequence that will bind MHC and induce an immune response. Computer programs exist wherein one can enter a specified amino acid sequence and the computer will predict, for example, which nine consecutive amino acids will bind MHC, such as HLA-A2.

SEQ ID NO: 1, which is 102 amino acids in length, has not been disclosed in the prior art.

4. The level of skill of one of ordinary skill in the art

The level of skill of the average molecular biologist or immunologist is high.

5. The level of predictability in the art

Computer programs can be used to predict which eight to ten consecutive amino acids of a specified polypeptide are likely to bind MHC. These programs rank polypeptides in order of predicted strength of the binding. Once the polypeptides are identified, a biological assay can be used to confirm that the eight to ten consecutive amino acids actually bind MHC.

6. The amount of direction provided in the application

There is considerable direction provided in the application. The amino acid sequence of PAGE4 is provided as SEQ ID NO: 1 of the specification. This amino acid sequence is 102 amino acids in length. Immunogenic peptides are clearly described in the specification. For example, immunogenic peptides, such as peptides that bind MHC are disclosed in the specification on page 7, line 35 to page 8, line 25, and on page 20, line 1 to page 22, line 5. The specification also discloses that epitopes of use are 8-10 amino acids in length and have anchoring residues. Specific configurations of use are disclosed, such as wherein the PAGE4 polypeptides is 9 or 10 amino acids in length and includes binding motifs for HLA-A2 (see, for example, page 8, lines 30-37, page 20, to page 21, line 2, and page 21, lines 15-19), such as those peptides that have specific anchoring residues in the second position and a positively charged amino acid at the position nine (see page 20, line 20 to page 21, line 2). The selection of binding motifs that bind HLA-A2 is further described on page 28, line 25 to page 29, line 29. Methods and computer based programs for predicting MHC binding motifs (immunogenic epitopes) were disclosed in the specification (for example, see page 8, lines 12-25 and page 21, line 34 to page 22, line 5), and were well known to those of skill in the art at the time the provisional application was filed (see for example, Parker et al., Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-chains. J Immunol 152:163-75, 1994). In addition, biological methods of testing whether a specific epitope is immunogenic are also provided (for example, see page 8, lines 1-4 and page 21, lines 3-12 and lines 20-29).

7. The existence of working examples

SEQ ID NO: 1 is provided in the specification, as are experimental examples describing the isolation of the nucleic acid encoding SEQ ID NO: 1 and expression vectors encoding SEQ ID NO: 1. A fragment of PAGE4 (15 amino acids) that can be used to produce antibodies is disclosed on page 41.

8. The quantity of experimentation needed to make or use the invention.

Synthetic polypeptides can be produced by automated machinery. In addition, a number of expression vectors are known in the art (and commercially available) that can be used to produce the claimed polypeptides. Thus, only very limited routine experimentation is required to produce polypeptides comprising SEQ ID NO: 1 and/or consisting of SEQ ID NO: 1.

To identify polypeptides consisting of eight to ten amino acids in length that bind MHC, the sequence must be entered into a computer program to identify epitopes of interest. There are programs that are publicly available for the identification of epitopes that bind MHC (for example, free access to the program referred to in the specification, namely Parker et al., Scheme for ranking potential HLA-A2 binding peptides based on independent binding of individual peptide side-chains. J Immunol 152:163-75, 1994, is provided on the internet at http://bimas.dcrt.nih.gov/molbio/hla_bind/). As discussed above, these methods for predicting MHC binding were well known to those of skill in the art at the time the provisional application was filed (see for example, Parker et al., *supra*). In addition, considerable supporting information is also provided in the specification, for example methods and computer based programs for predicting MHC binding motifs (immunogenic epitopes) are described on page 8, lines 12-25 and page 21, line 34 to page 22, line 5).

Once a polypeptide consisting of eight to ten consecutive amino acids of SEQ ID NO: 1 is identified using the program, this polypeptide must be synthetically produced. As noted above, the synthesis of short polypeptides is routine. Following synthesis, the polypeptide must is screened to demonstrate it binds MHC and can induce a T cell response. Biological methods to test whether a specific epitope is immunogenic are provided in the specification (for example, see page 8, lines 1-4 and page 21, lines 3-12 and lines 20-29). One of skill in the art can perform these assays, as evidenced in the Declaration of Dr. Pastan, submitted herewith. Thus, given the very complete disclosure provided by the specification, only limited experimentation is required.

Applicants submit that this Wands analysis supports the finding that the pending claims are supported by the specification. With regard to limiting the growth of a malignant cell using the claimed peptides, Applicants submit that the specification is fully enabling, see for example page 22, line 1 to 25, line 10. Moreover, as discussed above, the enclosed declaration of Dr. Pastan documents that, using methods such as those described in the specification, documenting that a polypeptide of nine consecutive amino acids of SEQ ID NO: 1 can be used to activate cytotoxic T cells. These T cells can lyse prostate cancer cells *in vitro*. This evidence supports the assertion that the specification is fully enabling for the use of the claimed polypeptides.

The Office action states on page 22, that even if the Applicant could overcome the rejections under 35 U.S.C. § 112, first paragraph, and even if the polypeptides could be used for inhibiting the growth of malignant cells, then claims 14-15 and 17-18 are rejected for encompassing a method for inhibiting the growth of a malignant cell expressing variants of PAGE4 having the amino acid sequence set forth as SEQ ID NO: 1 (see page 22 of the Office action).

In view of the above remarks, and the Declaration of Dr. Pastan, Applicants believe that they have overcome the rejections under 35 U.S.C. § 112, first paragraph. Claims 14-15 and 17-18 have been limited to malignant cells expressing SEQ ID NO: 1, thereby rendering the rejection moot.

The Office action further states that the specification only describes that PAGE4 is expressed in uterine and prostate cancers, and thus alleges that the claimed methods are not enabled for inhibiting the growth of any cancer. Applicants respectfully disagree with this rejection, and note that prostate and uterine cancer can be considered to be two species supporting a claim to a genus, namely cancer. However, solely to advance prosecution, the claims have been amended to be limited to prostate and uterine cancer, rendering the rejection moot. Applicants reserve the right to prosecute any deleted subject matter in a continuation application.

Applicants would like to put on the record that the subject matter of claims 14-15 and 17-18, as applied to all types of cancer, has clearly been searched by the U.S. Patent and Trademark Office in preparing the first Office action; a restriction requirement is inappropriate.

Rejection Under 35 U.S.C. § 102(e)

Claims 1-2, 53 and 55 are rejected under 35 U.S.C. § 102(e) as allegedly being anticipated by U.S. Patent Application Publication No. 2004/0248256A1. The Office action states that this publication is effective as a reference as of the filing date of one of the parent provisional applications, namely May 7, 1998.

Submitted herewith is a Declaration Under 35 U.S.C. § 1.131, documenting that prior to May 7, 1998, the inventors obtained the amino acid sequence set forth as SEQ ID NO: 2 and conceived of using immunogenic compositions for the treatment of cancer prior. The declaration is signed by Dr. Lee and Dr. Pastan.

This declaration was prepared following a review of the NIH's files. As discussed with Examiner Davis on March 13, 2006, the Applicants are aware that Dr. Vasmatzis must sign the declaration. However, Dr. Vasmatzis, who has relocated to the Mayo Clinic, is traveling and will not return until March 13, 2006. The undersigned representative has tried to contact Dr. Vasmatzis, and will forward the copy of the Declaration executed by Drs. Vasmatzis immediately upon receipt. It is the Applicants' understanding from the brief telephone interview that Examiner Davis will accept a copy of the declaration signed by Dr. Vasmatzis at a later date. The undersigned will make every effort to forward the Declaration executed by Dr. Vasmatzis expeditiously.

Conclusion

It is respectfully submitted that the present claims are in a condition for allowance. If any issues remain, the Examiner is requested to contact the undersigned attorney prior to issuance of the next Office action in order to arrange a telephone interview. It is believed that a brief discussion of the merits of the present application may expedite prosecution and allowance of the claims.

Respectfully submitted,

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